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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/163,089	09/29/1998	IAN F. C. MCKENZIE	5036-1	9586

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EXAMINER	
ZEMAN, ROBERT A	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 08/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/163,089	MCKENZIE ET AL.	
	Examiner	Art Unit	
	Robert A. Zeman	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 25 April 2005.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1,3-11,13-17,19-21,24-26,38 and 70 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,3-11,13-17,19-21,24-26,38 and 70 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 4-25-2005 has been entered.

The amendment and response filed on 4-25-2005 are acknowledged. Claims 1, 20, 21 and 70 have been amended. Claims 12 and 71-72 have been canceled. Claims 1, 3-11, 13-17, 24-26, 38 and 70 are pending and currently under examination.

The Declaration filed on 10-27-2004 has been fully considered.

Claim Objections Withdrawn

The objection to claim 71 under 37 CFR 1.75 as being a substantial duplicate of claim 70 is withdrawn. Cancellation of claim 71 has rendered the invention moot.

Claim Rejections Withdrawn

The rejection of claims 1, 3-17, 19-21, 24-26, 38 and 70-72 under 35 U.S.C. 112, first paragraph, the specification, while being enabling for immunoregulatory compositions comprising mannose receptor bearing cells, and a conjugate comprising MUC1 (antigen) and a carbohydrate polymer comprising mannose, wherein said carbohydrate polymer is a fully

oxidized carbohydrate polymer comprising free aldehydes, does not reasonably provide enablement for immunoregulatory compositions comprising mannose bearing cells and a conjugate comprising any antigen and a carbohydrate polymer comprising mannose, wherein said carbohydrate polymer is a fully oxidized polymer comprising free aldehydes is withdrawn in lieu of the rejection set forth below.

New Grounds of Rejection

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 5-11, 13-17, 19-21, 24-26, 38 and 70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for immunoregulatory compositions comprising mannose receptor bearing antigen presenting cells (i.e. macrophages and dendritic cells) and a conjugate comprising tumor antigens MUC1 and CRIPTO and a carbohydrate polymer comprising mannose, wherein said carbohydrate polymer is a fully oxidized carbohydrate polymer comprising free aldehydes, does not reasonably provide enablement for immunoregulatory compositions comprising any mannose bearing cells other than APCs and a conjugate comprising any tumor antigen other than MUC1 and CRIPTO and a carbohydrate polymer comprising mannose, wherein said carbohydrate polymer is a fully oxidized polymer comprising free aldehydes. In short the specification is enabling only for compositions comprising APCs and either MUC1 or CRIPTO tumor antigens.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The instant invention is drawn to compositions comprising isolated mannose receptor-bearing cells **and** a conjugate comprising a tumor antigen and a carbohydrate polymer comprising mannose, wherein said carbohydrate polymer is a fully oxidized carbohydrate polymer comprising free aldehydes. The rejected claims are drawn to compositions that are to be applied to animals/humans. People of skill in the art require documented evidence, that a benefit can be derived by the therapeutic application of a given substance. The specification provides ample evidence those compositions comprising mannose receptor-bearing antigen presenting cells (macrophages) and a conjugate comprising MUC1 and fully oxidized mannose polymer (Ox-M-FP) can be used to elicit a cytotoxic T cell response to MUCI. Moreover, the declaration filed 10-27-2004 demonstrates the efficacy of dendritic cells and a conjugate comprising CRIPTO and fully oxidized mannose polymer for eliciting a cytotoxic T cell response to CRIPTO. However, the instant specification fails to provide direction on what tumor antigens, other than MUCI and subsequently CRIPTO, and what other mannose receptor bearing cells other than antigen-presenting cells are capable of eliciting the claimed immune response. Applicant has failed to give direction on what conjugates, other than those comprised of MUCI or CRIPTO, antigen presenting cells bearing mannose receptors and fully oxidized mannose (Ox-M-FP), would meet the limitations of the instant claims and has provided no evidence the application of the any compositions other than those outlined above would elicit the requisite immune response. Moreover, the specification provides no guidance with regard to the use of mannose receptor-bearing cells that do not function as antigen presenting cells. For instance,

Lew et al. (J. Clin. Invest. 1994, Vol. 94, pages 1855-1863) disclose that lung smooth muscle cells have mannose receptors and that said receptors induce mitogenesis (see abstract). It is unclear how cells with the disclosed function of the mannose receptor-bearing cells could be used to elicit a cellular immune response. Given the lack of success in the art, the lack of working examples, and the unpredictability of the generation of a therapeutic response in a living organism, the specification, as filed, is not enabling for the use of all tumor antigens in conjunction with all mannose receptor-bearing cells to elicit a cellular immune response.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-11, 13-17, 19-21, 24-26, 38 and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over McKenzie et al. (EP 0 659 768 A2) in view of Koning et al. (WO 98/13378).

The aforementioned claims are based on immunoregulatory compositions comprising mannose receptor bearing cells. This limitation was not disclosed or enabled in the parent application. Consequently, the filing date of the instant application determines the availability of art under 35 U.S.C. 102(b).

The instant claims are drawn to immunoregulatory compositions comprising mannose receptor-bearing cells and a conjugate comprising a tumor antigen (MUCI) and a carbohydrate polymer (fully oxidized mannose). McKenzie et al. disclose a conjugate comprising a tumor antigen (mucin) and a carbohydrate polymer (mannose) that is used to induce cell-mediated immune responses (see abstract). McKenzie et al further disclose a conjugate which consists of the MUCI antigen and a fully oxidized mannose polymer (see pate 4, lines 19-20); the use of immune regulators such as GM-CSF, IL-3, and IL-4 (see page 5, lines 30-34); and that the antigen comprise repeating subunits of at least 5 amino acids (see page 3, lines 1-3). McKenzie et al. differs from the instant claims in that the claimed conjugate is not combined with mannose receptor-bearing cells at the time of administration to the patient or used for the *ex vivo* pulsing of the mannose receptor-bearing cells. Koning et al. disclose the mannosylated antigens to enhance the uptake and MHC restricted presentation of said antigens by mannose receptor-bearing cells (see abstract). Consequently, it would have been obvious for one of skill in the art to combine the antigen-mannose conjugate disclosed by McKenzie et al. with mannose receptor bearing cells as disclosed by Koning et al. since targeting a mannose receptor increases the

uptake efficiency of an antigen and its presentation by antigen presenting cells resulting in an increased ability to induce T-cells (see Koning et al. page 5). One would have had a high expectation of success since Koning et al disclose that the mannosylation of a variety of peptides and proteins led to an increased ability to induce a T-cell response (see pages 15-19 and Table 1).

Claims 1, 3-11, 13-17, 19-21, 24-26, 38 and 70 are rejected under 35 U.S.C. 1O3(a) as being unpatentable over McKenzie et al. (EP 0 659 768 A2) in view of Maraskovsky et al. (U.S. Patent 6,017,527).

The aforementioned claims are based on immunoregulatory compositions comprising mannose receptor bearing cells. This limitation was not disclosed or enabled in the parent application. Consequently, the filing date of the instant application determines the availability of art under 35 U.S.C. 102(b).

The instant claims are drawn to immunoregulatory compositions comprising mannose receptor-bearing cells and a conjugate comprising a tumor antigen (MUCI) and a carbohydrate polymer (fully oxidized mannose). McKenzie et al. disclose a conjugate comprising a tumor antigen (mucin) and a carbohydrate polymer (mannose) that is used to induce cell-mediated immune responses (see abstract). McKenzie et al further disclose a conjugate which consists of the MUCI antigen and a fully oxidized mannose polymer (see pate 4, lines 19-20); the use of immune regulators such as GM-CSF, IL-3, and IL-4 (see page 5, lines 30-34); and that the antigen comprise repeating subunits of at least 5 amino acids (see page 3, lines 1-3). McKenzie et al. differs from the instant claims in that the claimed conjugate is not combined with mannose receptor-bearing cells at the time of administration to the patient or used for the *ex vivo* pulsing

of the mannose receptor-bearing cells. Maraskovsky et al. the use of antigen expressing, activated mannose receptor-bearing cells (dendritic cells) to present tumor antigens to T cells. Moreover, Maraskovsky et al. disclose the use of cytokines in separate, sequential or simultaneous combinations with said activated cells (see abstract). Finally, Maraskovsky et al. disclose methods of inducing specific immune responses utilizing "antigen-pulsed" dendritic cells (see column 11). Consequently, it would have been obvious for one of skill in the art to combine the antigen-mannose conjugate disclosed by McKenzie et al. with the activated dendritic (mannose receptor bearing) cells as disclosed by Maraskovsky et al. in order to take advantage of the ability of dendritic cells to increase the immunogenicity of antigens. One would have had a high expectation of success since Maraskovsky et al disclose since activated dendritic cells can serve as effective agents for enhancing and targeting immune responses to tumor antigens (see column 1, lines 15-47).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ROBERT A. ZEMAN
PATENT EXAMINER

July 18, 2005